AMENDMENTS TO THE CLAIMS

1. (Withdrawn) A purified and isolated AMIGO nucleic acid comprising a nucleotide sequence that encodes a polypeptide comprising the amino acid sequence shown in SEQ ID NO:2, 4 or 6.

2. (Withdrawn) A purified and isolated nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:1, 3 or 5.

3. (Withdrawn) A purified and isolated nucleic acid comprising a recombinant nucleotide sequence comprising a nucleotide sequence shown in SEQ ID NO:1, 3 or 5 or a homolog or fragment thereof.

4. (Withdrawn) An expression construct comprising the nucleic acid according to claim 2 operatively linked to an expression control sequence, said expression construct capable of encoding an AMIGO polypeptide or variants thereof.

5. (Withdrawn) A host cell transformed or transfected with the expression construct of claim 4.

6. (Withdrawn) A host cell transformed or transfected with a polynucleotide wherein said polynucleotide includes a strand containing a human nucleotide sequence that hybridizes to a

DNA comprising the non-coding strand complementary to SEQ ID NO:1, 3 or 5, under the following hybridization conditions:

(a) hybridization at 42 °C for 20 hours in a solution containing 50% formamide, 5 X SSPE, 5 X Denhardt's solution, 0.1% SDS and 0.1 mg/ml denatured salmon sperm DNA; and

(b) washing the filter twice for thirty minutes at room temperature and twice for thirty minutes at 65 °C with a wash solution containing 1xSSC, and 0.1% SDS.

7. (Currently Amended) An isolated and purified ectodomain fragment of AMIGO polypeptide comprising amino acids 1-371 of the amino acid sequence of SEQ ID NO:2, amino acid sequence of SEQ ID NO:4 or amino acid sequence of SEQ ID NO:6.

8. (Withdrawn) Method of producing an AMIGO polypeptide according to claim 7, said method comprising the steps of:

culturing a host cell of claim 5 comprising a polynucleotide encoding said polypeptide operably associated with a promoter sequence such that the nucleic acid sequence encoding said polypeptide is expressed; and

isolating said polypeptide from said host cell or from a growth medium in which said host cell is cultured.

9. (Withdrawn) Method of producing antibodies comprising:

- immunising a mammal with the isolated and purified AMIGO protein of claim 7 or an antigenic fragment thereof.

10. (Withdrawn) Use of the isolated and purified AMIGO protein of claim 7 or an antigenic fragment thereof as an antigen.

11. (Withdrawn) An antibody produced by the method of claim 9.

12. (Withdrawn) The antibody of claim 11 which is labeled with a detectable label.

13. (Withdrawn) A kit of reagents for use in detecting the presence of AMIGO or allelic variant thereof in a biological sample, comprising

- a container; and in said container:

- a compound, preferably labeled, capable of detecting AMIGO or allelic variants thereof.

14. (Withdrawn) The kit according to claim 13, wherein said compound is a primer or probe.

15. (Withdrawn) The kit according to claim 13, wherein said compound is an antibody as defined in claim 11.

16. (Withdrawn) The kit according to claim 13 for assessing the predisposition of an individual to a condition mediated by variation or dysfunction of AMIGO.

17. (Withdrawn) The kit according to claim 16 further comprising instructions for using the kit.

18. (Withdrawn) A transgenic non-human animal containing a human or murine AMIGO gene as a transgene.

19. (Withdrawn) A transgenic non-human animal containing a transgene or insertion disrupting expression of an AMIGO gene or a homolog thereof.

20. (Currently Amended) A pharmaceutical ~~compound~~ composition comprising ~~AMIGO nucleic acid molecule, AMIGO protein, AMIGO peptide fragment, AMIGO fusion protein, AMIGO agonists, AMIGO antagonists or anti-AMIGO antibody~~ amino acids 1-371 of SEQ ID NO:2 or an antibody specifically binding to amino acids 1-371 of SEQ ID NO:2.

21. (Withdrawn) Method for treatment of a condition dependent on AMIGO wherein a pharmaceutically effective amount of the compound of claim 20 is administered to a patient in need of such treatment.

22. (Withdrawn) Method for affinity purification of ligand that binds to the AMIGO comprising the following steps: a) contacting a source of AMIGO receptor with an immobilized AMIGO under conditions whereby the AMIGO receptor to be purified is selectively adsorbed onto the immobilized AMIGO; (b) washing the immobilized AMIGO and its support to remove

non-adsorbed material; and (c) eluting the AMIGO receptor molecules from the immobilized AMIGO to which they are adsorbed with an elution buffer.

23. (Withdrawn) A method for identifying a modulator of binding between an AMIGO receptor and an AMIGO receptor, comprising steps of:

(a) contacting an AMIGO receptor composition with an AMIGO composition in the presence and in the absence of a putative modulator compound;

(b) detecting binding between AMIGO receptor and the AMIGO receptor in the presence and absence of the putative modulator; and

(c) identifying a modulator compound in view of decreased or increased binding between the AMIGO receptor and the AMIGO receptor in the presence of the putative modulator, as compared to binding in the absence of the putative modulator.

24. (Withdrawn) A method according to claim 23, further comprising a step of:

(d) making a modulator composition by formulating a modulator identified according to step (c) in a pharmaceutically acceptable carrier.

25. (Withdrawn) A method according to claim 24, further comprising a step of:

(e) administering the modulator composition to an animal that comprises cells that express the AMIGO receptor, and determining physiological effects of the modulator composition in the animal.

26. (Withdrawn) A method according to claim 23, wherein the AMIGO receptor composition comprises a member selected from the group consisting of:

(a) a purified polypeptide comprising a AMIGO receptor extracellular domain fragment that binds the AMIGO;

(b) a phospholipid membrane containing AMIGO receptor polypeptides; and

(c) a cell recombinantly modified to express increased amounts of an AMIGO receptor on its surface.

27. (Withdrawn) A method according to claim 23, wherein the AMIGO receptor composition comprises an AMIGO receptor extracellular domain fragment bound to a solid support.

28. (Withdrawn) A method according to claim 23, wherein the AMIGO receptor composition comprises an AMIGO receptor extracellular domain fragment fused to an immunoglobulin Fc fragment.

29. (Withdrawn) A method according to claim 23, wherein the AMIGO receptor is selected from the group consisting of a mammalian AMIGO, AMIGO2, and AMIGO3.

30. (Withdrawn) A method according to claim 23, wherein the AMIGO receptor is human.

31. (Withdrawn) A method according to claim 23, wherein the AMIGO composition comprises a member selected from the group consisting of:

(a) a purified polypeptide comprising an AMIGO fragment that binds the AMIGO receptor;

(b) a phospholipid membrane containing AMIGO polypeptides; and

(c) a cell recombinantly modified to express increased amounts of an AMIGO on its surface.

32. (Withdrawn) A method according to claim 23, wherein the AMIGO composition comprises an AMIGO extracellular domain fragment bound to a solid support.

33 (Withdrawn) A method according to claim 23, wherein the AMIGO composition comprises an AMIGO extracellular domain fragment fused to an immunoglobulin Fc fragment.

34. (Withdrawn) A method according to claim 23, wherein the AMIGO is human.

35. (Withdrawn) A method according to claim 23, wherein the AMIGO receptor composition comprises a cell recombinantly modified to express increased amounts of an AMIGO receptor on its surface, and wherein the detecting step comprises measuring an AMIGO binding-induced physiological change in the cell.

36 (Withdrawn) A method according to claim 23, wherein the AMIGO composition comprises a cell recombinantly modified to express increased amounts of an AMIGO on its surface, and wherein the detecting step comprises measuring an AMIGO binding-induced physiological change in the cell.

37. (Withdrawn) A method for screening for selectivity of a modulator of binding between an AMIGO and an EGFR, comprising steps of:

a) contacting an AMIGO receptor composition with an EGFR composition in the presence and in the absence of a compound that modulates binding between the AMIGO receptor and EGFR receptor; and

b) detecting binding between the AMIGO receptor composition and the EGFR receptor composition in the presence and absence of the modulator compound,

c) identifying the selectivity of the modulator compound in view of decreased or increased binding between the AMIGO receptor and the EGFR receptor in the presence as compared to the absence of the modulator, wherein increased selectivity of the modulator for modulating AMIGO EGFR binding correlates with decreased differences in AMIGO- EGFR binding.

38. (Withdrawn) A method of modulating growth, migration, axonal growth, myelination, fasciculation or proliferation of cells in a mammalian organism, comprising a step of:

(a) identifying a mammalian organism having cells that express a AMIGO receptor and/or EGFR; and

(b) administering to said mammalian organism a composition, said composition comprising an agent selected from the group consisting of:

(i) a polypeptide comprising an AMIGO receptor that binds to the AMIGO receptor and/or EGFR, or a nucleic acid encoding said polypeptide;

(ii) a polypeptide comprising a fragment of the AMIGO, wherein the polypeptide and fragment retain AMIGO binding characteristics of the AMIGO, or a nucleic acid encoding said polypeptide;

(iii) an antibody that specifically binds the polypeptide of (i) or (ii) in a manner that inhibits the polypeptide from binding the AMIGO receptor and/or EGFR, or a fragment of the antibody that specifically binds the polypeptide of (i) or (ii);

(iv) a polypeptide comprising an antigen-binding fragment of (iii) and that inhibits the polypeptide of (i) or (ii) from binding the AMIGO receptor and/or EGFR;

(v) a molecule that selectively inhibits AMIGO binding to the AMIGO receptor without inhibiting AMIGO binding to the EGFR receptor; and

(vi) a molecule selectively binding to the AMIGO receptor and the EGFR receptor;

wherein the composition is administered in an amount effective to modulate growth, migration, or proliferation of cells that express AMIGO in the mammalian organism.

39. (Withdrawn) A method according to claim 38, wherein the mammalian organism is human.

40. (Withdrawn) A method according to claim 38, wherein the cells comprise neuronal cells.

41. (Withdrawn) A method according to claim 38, wherein the organism has a disease characterized by aberrant growth, migration, or proliferation of neuronal cells/neuronal extensions.

42. (Withdrawn) A method according to claim 38, wherein the conditions comprises a neuronal trauma.

43. (Withdrawn) A method according to claim 38, further comprising administering a second agent to the patient for modulating neuronal growth, migration, regeneration or proliferation, said second agent selected from the group consisting of: an antibody that specifically binds with any of the foregoing polypeptides, an antibody that specifically binds with a receptor for any of the foregoing polypeptides, or a polypeptide comprising an antigen binding fragment of such antibodies.

44. (Withdrawn) A method according to claim 38, wherein the AMIGO extracellular fragment is conjugated with Fc domain.

45. (Withdrawn) A method according to claim 44, wherein rat AMIGO Fc fusion protein sequences have been replaced essentially with the human AMIGO and Fc sequences

46. (Withdrawn) A polypeptide according to claim 38, for use in the manufacture of a medicament for the treatment of diseases characterized by aberrant growth, migration, regeneration or proliferation of cells that express an AMIGO receptor.

47. (Withdrawn) Method according to claim 38 wherein neuronal cells are selected from the group consisting of: hippocampal cells, cerebral cells, cerebellar cells, neuronal trauma cells, glial scar cells, spinal cord cells, optic nerve cells, retina cells, kidney cells, and cells acting during fasciculation, guidance, growth, or myelination.

48. (Withdrawn) A method of modulating cancer, tumour growth or metastasis in a mammalian organism, comprising a step of:

(a) identifying a mammalian organism having cells that express an AMIGO receptor and/or EGFR; and

(b) administering to said mammalian organism a composition, said composition comprising an agent selected from the group consisting of:

(i) a polypeptide comprising an AMIGO receptor that binds to the AMIGO receptor and/or EGFR, or a nucleic acid encoding said polypeptide;

(ii) a polypeptide comprising a fragment of the AMIGO, wherein the polypeptide and fragment retain AMIGO binding characteristics of the AMIGO, or a nucleic acid encoding said polypeptide;

(iii) an antibody that specifically binds the polypeptide of (i) or (ii) in a manner that inhibits the polypeptide from binding the AMIGO receptor and/or EGFR, or a fragment of the antibody that specifically binds the polypeptide of (i) or (ii);

(iv) a polypeptide comprising an antigen-binding fragment the (iii) and that inhibits the polypeptide of (i) or (ii) from binding the AMIGO receptor and/or EGFR;

(v) a molecule that selectively inhibits AMIGO binding to the AMIGO receptor without inhibiting AMIGO binding to the EGFR receptor; and

(vi) a molecule selectively binding to the AMIGO receptor and the EGFR receptor;

wherein the composition is administered in an amount effective to modulate cancer growth or metastasis of cells that express AMIGO in the mammalian organism.

49. (Withdrawn) A method according to claim 48, wherein the mammalian organism is human.

50. (Withdrawn) A method according to claim 48, wherein the cells comprise glioma, glioblastoma, astrocytoma, anaplastic astrocytoma, ependymomas, oligodendrogliomas, medulloblastomas, meningiomas, schwannomas, craniopharyngiomas, germ cell tumors, pineoblastoma, pineocytoma, germinoma cells, lung carcinoma, breast carcinoma, ovarian

carcinoma, colorectal carcinoma, bladder carcinoma, pancreatic carcinoma, squamous cell carcinoma, or renal carcinoma cells.

51. (Withdrawn) A method according to claim 48, wherein the organism has a disease characterized by cancer or metastasis.

52. (Withdrawn) A method according to claim 51, wherein the condition comprises a brain tumor.

53. (Withdrawn) A method according to claim 48, further comprising administering a second agent to the patient for modulating cancer growth or metastatic growth of cancer, said second agent selected from the group consisting of: an antibody that specifically binds with any of the foregoing polypeptides, an antibody that specifically binds with a receptor for any of the foregoing polypeptides, or a polypeptide comprising an antigen binding fragment of such antibodies.

54. (Withdrawn) A method according to claim 48, wherein the AMIGO extracellular fragment is conjugated with Fc domain.

55. (Withdrawn) A method according to claim 48, wherein rat AMIGO Fc fusion protein sequences have been replaced essentially with the human AMIGO and Fc sequences

56. (Withdrawn) Method for treatment of cancer or metastatic growth of cancer cells selected from the group consisting of: glioma, glioblastoma, astrocytoma, anaplastic astrocytoma, ependymomas, oligodendrogliomas, medulloblastomas, meningiomas, schwannomas, craniopharyngiomas, germ cell tumors of germinoma cells, lung carcinoma, breast carcinoma, ovarian carcinoma, colorectal carcinoma, bladder carcinoma, pancreatic carcinoma, squamous cell carcinoma, and renal carcinoma, comprising a step of administering to a subject in need of such treatment the compound as claimed in claim 20.

57. (Withdrawn) Method for treatment of neuronal cells selected from the group consisting of: hippocampal cells, cerebral cells, cerebellar cells, neuronal trauma cells, glial scar cells, spinal cord cells, optic nerve cells, retina cells, kidney cells, and cells acting during fasciculation, guidance, growth, or myelination, comprising a step of administering to a subject in need of such treatment the compound as claimed in claim 20.

58. (Currently Amended) A ~~polypeptide or a nucleic acid encoding said polypeptide, said polypeptide comprising a fragment of an AMIGO that binds to an AMIGO receptor, for use in the manufacture of a medicament for the treatment of~~ method of treating diseases characterized by aberrant growth, migration, regeneration or proliferation of cells that express an AMIGO receptor, comprising administering to a subject in need thereof an effective amount of the composition according to claim 20.

59. (Withdrawn) A method of modulating the phosphorylation of a human epidermal growth factor receptor in cells or tissues comprising contacting said cells or tissues with the AMIGO compounds.

60. (Withdrawn) The method of claim 59, wherein said AMIGO compounds comprises AMIGO peptides encoded a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:5.

61. (Withdrawn) The method of claim 59, wherein said AMIGO compounds comprise an anti-AMIGO antibody.

62. (New) An isolated and purified human AMIGO1 polypeptide consisting of amino acids 1-371 set forth in SEQ ID NO:2.

63. (New) A method of producing a human AMIGO1 ectodomain fragment, wherein said method comprises:

a) providing a modified nucleic acid encoding said human AMIGO1 polypeptide, comprising SEQ ID NO:1, wherein nucleic acids encoding a transmembrane domain of said human AMIGO1 polypeptide are removed from SEQ ID NO:1;

b) expressing the modified nucleic acid obtained in step a) in a host cell to produce a human AMIGO1 ectodomain fragment; and

c) isolating and purifying the human AMIGO1 ectodomain fragment from the host cell or from a growth medium in which the host cell is cultured.

64. (New) The method according to claim 63, wherein said human AMIGO1 ectodomain fragment consists of amino acids 1-371 of SEQ ID NO:2.